

Pliny's pharmacopoeia or the Roman treat

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Pliny's pharmacopoeia is considered to be the cradle of pharmacotherapy. Its compilation, accessibility and distribution on a larger scale then ever before took care of the spread of knowledge, which contributed to its name and fame throughout the ages. References to a (nonspecified) cardiac diagnosis are discussed with special interest in glycosides, flavonoids, alkaloids and synergy in drug action. The importance of systems biology leading to a scientific-based herbal medicine is underlined as a major issue in future pharmacotherapy, bridging more than 2½ thousand years of pharmacological intervention. (*Neth Heart J* 2007;15:118-20.)

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n 'matters of the heart' general advice is as old as mankind. Nevertheless, medical prescriptions also go back a long way and ancient civilisations like Egypt and Samaria could rely on some sort of pharmacopoeia. Knowledge, however, was scattered and also depended on the regional availability of herbs

After the Romans conquered Greece (completed in about 150 BC), there was an increase in nationalism following the steady influx of Greek scholars and physicians into Roman society. Encyclopaedism, as a particular form of nationalism, gave expression to the need felt at that time for propagation of an own Roman identity in writing about social, religious, political, scientific and medical matters. Encyclopaedias (and pharmacopoeia) were also compiled to implement existing knowledge in daily practice and to take the wind out of the

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Correspondence to: C. van Tellingen Department of Cardiology, St Franciscus Hospital, PO Box 999, 4700 AZ Roosendaal, the Netherlands E-mail: cvantellingen@dukebox.demon.nl Greek sails as far as possible. Therefore encyclopaedias were not intended to promote new ideas or new techniques but presented what could be called the first attempt in history to develop a new concept of mass knowledge industry. This concept is clearly stated in Pliny the elder's Naturalis Historiae XXIX19: 'Aliena memoria salutamus, aliena vivimus opera, alienis oculis agnostimus or: we welcome unfamiliar memories, we preserve unfamiliar work, we observe with unfamiliar eyes' (figure 1).

Pliny's pharmacopoeia

Even in our modern times, a medical prescription is still charged with some kind of magical power, despite the fact that herbal medicine as a modus operandi has been replaced by a glamorous market full of specialities. Nevertheless, active herbal constituents are sometimes the precursors of modern drugs and for that reason one should not lightly dismiss the potential of herbal medicines in general. Pliny lived and worked in the first century AD, served three emperors and was renowned for his integrity. As a member of the imperial council, he managed to write enormous amounts of material. His Naturalis Historiae, first published in 77 AD, is a massive compilation in 37 books of the prevailing knowledge of social, religious, political, scientific and medical matters. The underlying thread of his work was anthropocentrism. In his pharmacopoeia, some 20 herbal species are related to a (nonspecified) cardiac diagnosis (table 1).

Discussion

Nowadays, herbal medicine has been pushed away to the outer limits of regular medicine and has become the domain of alternative healers and fortune seekers living off various lifestyle programmes. Nevertheless, herbalism is the cradle of pharmacology and therefore studying its nature and development, especially in ancient times, remains of great importance and may be particularly helpful in understanding thought and reason at that time. This, in turn, could lead to new lines of development and research, which may be beneficial in our modern times too.

It is amazing to see that some of the constituents of Roman traditional medicine featured in the pharmaceutical guide



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until the 1930s. Atropine of course (for Adam-Stokes), but also allium sativum (for atherosclerosis) viscum album (for hypertension) aconitum and helleborus niger (for rheumatism) shared the therapeutic compendium at that time.1 In the decades thereafter more and more pharmaceutical specialities were developed and molecular pharmacology targeting one receptor soon dominated the therapeutic landscape. During this process the possibilities and additional value of complex chemical compounds such as herbs, (inter)acting in sometimes mysterious ways, were systematically neglected, not to say banished as undesirable side effects. Nowadays, synergy between different pharmaceutical compounds has regained new interest, especially in the approach to complex multifactorial diseases such as the metabolic syndrome.² Furthermore engineering sciences have found a useful application in biology, facilitating the beginning of a process of comprehending the interaction between genetics, the risk of developing disease and drug efficacy and action.

This concept of systems biology as a way to integrate data from a variety of sources has led to a better understanding of the interaction of genes with their environment. Beside comprehension, it enables the study of living systems from a holistic perspective based on the profiling of a multitude of



Figure 1. Pliny's Naturalis Historiae, published in 1669.

Latin name	Scientific name	Common name	(Alleged) action
Chelidonium	Chelidonia majus	Celandine	Laxative and diuretic; against jaundice and dropsy
Cytisus	Cytisis laburnum	Laburnum	Used in homoeopathy
Veratrum	Helleborus niger	Christmas rose	In smaller doses diuretic but uncertain in action; requires great caution
Laurus	Laurelia	Laurel	For rheumatism and slow digestion
Marrubium	Marrubium vulgaris	Horehound	For coughs in general, bronchitis, colds and feverish conditions
Aconitumeurs	Aconitum napellus	Monkshood	For rheumatism, gout, nervous pains, fever. Is diuretic and sudorific
llex	llex aquifolium	Holly berries	Exceedingly good in dropsy and colic. In higher dose purgative and emetic
Scilla	Urginea maritime	Sea onion	Contains cardiac glycosides/ flavonoids; used as emetic and for heart ailments
Genista	Genista sphaerocarpus	Broom	As diuretic and purgative especially in dropsy and liver disorders
Lupinus	Lupinus albus	White Iupine	Anthelminthic, diuretic and emmenogogue
Veratrum	Veratrum album	White hellebore	Contains alkaloids; used to treat hypertension in the 1950s and 1960s
Murtus	Myrtus communis	Myrtle	Diabetes mellitus
Ruta	Ruta graveolens	Rue	Oligomenorrhoea and amenorrhoea
Alium	Allium sativum	Garlic	Hypertension, arteriosclerosis, antiseptic acts favourably on the metabolic process
Anagyris foeta	Anagyris foetida	Bean trefoil	Homoeopathy
Strychnon	Atropa belladonna	Atropine	Anticholinergic
Hyoscyamos	Hyoscyamus albus	Atropine	Anticholinergic
Mandragoras	Mandragona vemalis	Atropine	Anticholinergic
Strychnon	Solarea nigra	Atropine	Anticholinergic
Strychnon	Datura stramonium	Atropine	Anticholinergic

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biochemical components. Application possibilities are tailored drug design but also the use of a multiple drug system, giving natural product research a new perspective in the form of a scientific-based herbal medicine, bridging 2½ thousand years of pharmacotherapy. This trend may well be applicable to a multifactorial determined condition as heart failure too. Henceforth, it could be worthwhile to look into some of the constituents of traditional Roman medicine presented here. In doing so, a systematic approach is necessary and therefore we have to go way back in time to find a reliable source, not contaminated with all sorts of commercial side issues. Lacking evidence-based guidance, objectivity is then of the utmost importance.

At first sight the constituents of Pliny's pharmacopoeia seem rather primitive with (hy)dropsy as the predominant cardiac diagnosis. A number of drugs are alike in their more or less purgative and diuretic action and in the meantime some have become obsolete. However, a minority, containing specific compounds such as alkaloids, flavonoids and glycosides, are of interest and are still under investigation in the present day. In ancient medicine, the view was prevalent that in hydropsy, patients were always thirsty, while drinking did nothing to alleviate their thirst but even worsened the situation. So purgatives and diuretics seemed rational and applicable at the time. Ancient Egyptians and later on the Romans used plants containing cardiac glycosides as emetics and for heart disease. At that time digitalis was considered to be poisonous and was sometimes used to contaminate the water supply of opposing forces in a state of war. For therapeutic use, they relied on urginea maritima with scillaglycoside and flavonoids as active substances. In comparison with digitalis, there is minimal chance of accumulation.

Veratrum alkaloids were used in the treatment of hypertension until the 1950s and 1960s. Nowadays the poisonous aspect of this plant easily mistaken for the yellow gentian used in beverages is of some importance.⁵ Recently, attention was drawn to the beneficial effects of the preoperative use of flavonoid on different organ functions. At least in rats, post-operative kidney function was better preserved and apoptosis in the intestine decreased.⁶ Furthermore, significant antioxidant activity seems to attenuate myocardial dysfunction provoked by reperfusion ischaemia.⁷ In specified clinical circumstances natural synergy, as is the case in urginea maritima, containing flavonoids and scillaglycoside with its inotropic, antiarrhythmic and vaso-active action, not to say neuro-

humoral modulation,⁸ need not be deleterious at all. With a sense of understatement one could then argue for a full circle with herbal medicine in antiquity.

Obviously a multitarget approach is preferable in multifactorial disarrangement. Such an approach will eventually surpass the *one target one compound* principle of modern day pharmacology, especially when the effects of pharmacotherapeutic intervention can be measured simultaneously in multiple endpoints, as for instance is the case in nutritional science which has to deal with the multiple effects of numerous nutrients at the same time.

Conclusion

So by all means, let us go back to the future despite the fact that the difficulties in substantiating this intent are numerous and at times it seems to be little more than wishful thinking. However, because the reductionistic approach to single active components is more than likely lacking efficaciousness and activity in highly complex living systems as humans with an internal ecosystem of diverse microbiota and parasites that have interactive metabolic processes, the notion of synergy in drug action could well be the only road to success in the time to come. Nevertheless and although synergy as a concept is tempting, as yet we had better stick to the words of apostle Paul: 'prove all things and hold fast that which is good', despite the old proverb which states: 'When in Rome, do as the Romans do'.

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